

**REMARKS**

Upon entry of the present amendments, claims 23-27 will be pending in this application. Claims 28-57, which were previously withdrawn as directed to a non-elected invention, are cancelled herein, without prejudice or disclaimer, in favor of a divisional application. Claim 23, the sole remaining independent claim, is amended herein. No new matter is introduced.

Applicants gratefully acknowledge the Examiner's withdrawal of the § 102(b) rejections over U.S. Pub. 2002/0022622 ("Wagle"). Applicants respectfully request reconsideration of the remaining § 103 rejections.

Briefly, the Examiner acknowledges that "Wagle does teach an infinite number of species as drawn to the compound of formula I . . . and does not anticipate the 2-amino-4,5-dimethylthiazole of the instant application" [OA, at p. 2], but contends that Wagle discloses "2-amino-5-methylthiazole and 2-amino-4-methylthiazole" and that it "is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results." [OA, at p. 4].

First, Applicants submit that the Examiner has failed to raise a prima facie case of obviousness of the instantly claimed composition because the Examiner has not provided a sufficient rationale for modifying the 2-amino-5-methylthiazole and 2-amino-4-methylthiazole compounds of Wagle. The Examiner's mere statement that "is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification" is legally incorrect, and does not constitute a sufficient rationale for making such modification.

While in some instances a "*prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities" (MPEP §2144.09), there is no such per se rule. Rather, even true homology (which substitution of methyl for hydrogen is not), "should not be automatically equated with *prima facie* obviousness because the claimed invention and the prior art must each be viewed 'as a whole.'" MPEP §2144.09. Accordingly, the Examiner should consider "the nature and significance of the differences between the prior art and the claimed invention" MPEP §2144(II)(A)(4)(c). For example, as stated in the MPEP, "the gain or loss of even one methyl group can destabilize the structure" of a protein "if close packing is required in the interior of domains." *Id.* Thus, in

analyzing whether substitution of methyl for hydrogen would have been prima facie obvious, there must be a “reasonable expectation of similar properties in structurally similar compounds” (MPEP §2144.09), and the Examiner must “[c]onsider the predictability of the technology” because if “the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties” MPEP §2144(II)(A)(4)(e).

Applicants note that in the Office Action dated April 18, 2007, the Examiner rejected the pending claims as lacking enablement under §112, first paragraph, due in part to the “lack of working example presented in the specification as filed showing that all compounds of the formula 1 inhibit AGE formation.” [April 18, 2007 OA, at p. 4]. The Examiner stated therein, that a “lack of a working example is a critical factor to be considered, especially in a case involving **an unpredictable and undeveloped art.**” *Id.* Having previously determined that the instant art is “unpredictable and undeveloped,” the Examiner should consider the §103 issues under this same state of the art. Applicants submit that there is no motivation to modify Wagle in the manner suggested for at least the reason that the Examiner has already indicated that it would not be predictable that the instant composition would have similar properties as the closest compounds of Wagle.

Moreover, even assuming that the Examiner has made out a prima facie case of obviousness, the instant specification provides data showing that the claimed composition possesses the unexpected property of inhibiting glucose oxidase, and the independent claim has been amended to recite a “composition for topical application to the skin for inhibiting glucose oxidase” which comprises the subject compound in an “effective amount for inhibiting glucose oxidase.” Example 3 on page 11 of the application describes the results of glucose oxidase inhibition using a commercially available glucose oxidase kit wherein production of hydrogen peroxide was reduced by greater than 60% in the presence of 2-amino-4,5-dimethylthiazole HCl as compared to a control sample. This unexpected property of 2-amino-4,5-dimethylthiazole HCl is not remotely contemplated by Wagle. As the Federal Circuit recently held in In re Dillon, 2007 WL 2433841 (Fed. Cir. August 29, 2007), “[w]hile a statement of intended use may not render a known composition patentable, the claimed composition was not known, and whether it would have been obvious depends upon consideration of the rebuttal evidence” and “[s]uch a use and unexpected property cannot be ignored.” Applicants submit that this beneficial property and

use (inhibiting glucose oxidase) of the hitherto unknown compositions of the invention further highlights the non-obviousness of the claims and rebuts any prima facie case of structural obviousness.

Based on the foregoing, Applicants submit that the present claims are not obvious over Wagle, taken alone or in combination with Gould, on which the Examiner relies only for the teaching of hydrochloride salts generally. Having distinguished independent claim 23 from the art of record, Applicants submit that the claims dependent therefrom are patentable for at least the same reasons but reserve the right to separately argue the patentability of those claims in the future, if necessary.

**CONCLUSION**

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendments and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided.

Respectfully submitted,

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